NTP TECHNICAL REPORT

ON THE

TOXICOLOGY AND CARCINOGENESIS

STUDIES OF

FURFURYL ALCOHOL

(CAS NO. 98-00-0)

IN F344/N RATS AND B6C3F$_1$ MICE

(INHALATION STUDIES)

February 1999

NATIONAL TOXICOLOGY PROGRAM
P.O. Box 12233
Research Triangle Park, NC 27709

NTP TR 482

NIH Publication No. 99-3972

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
National Institutes of Health

FOREWORD

The National Toxicology Program (NTP) is made up of four charter agencies of the U.S. Department of Health and Human Services (DHHS): the National Cancer Institute (NCI), National Institutes of Health; the National Institute of Environmental Health Sciences (NIEHS), National Institutes of Health; the National Center for Toxicological Research (NCTR), Food and Drug Administration; and the National Institute for Occupational Safety and Health (NIOSH), Centers for Disease Control. In July 1981, the Carcinogenesis Bioassay Testing Program, NCI, was transferred to the NIEHS. The NTP coordinates the relevant programs, staff, and resources from these Public Health Service agencies relating to basic and applied research and to biological assay development and validation.

The NTP develops, evaluates, and disseminates scientific information about potentially toxic and hazardous chemicals. This knowledge is used for protecting the health of the American people and for the primary prevention of disease.

The studies described in this Technical Report were performed under the direction of the NIEHS and were conducted in compliance with NTP laboratory health and safety requirements and must meet or exceed all applicable federal, state, and local health and safety regulations. Animal care and use were in accordance with the Public Health Service Policy on Humane Care and Use of Animals. The prechronic and chronic studies were conducted in compliance with Food and Drug Administration (FDA) Good Laboratory Practice Regulations, and all aspects of the chronic studies were subjected to retrospective quality assurance audits before being presented for public review.

These studies are designed and conducted to characterize and evaluate the toxicologic potential, including carcinogenic activity, of selected chemicals in laboratory animals (usually two species, rats and mice). Chemicals selected for NTP toxicology and carcinogenesis studies are chosen primarily on the bases of human exposure, level of production, and chemical structure. The interpretive conclusions presented in this Technical Report are based only on the results of these NTP studies. Extrapolation of these results to other species and quantitative risk analyses for humans require wider analyses beyond the purview of these studies. Selection *per se* is not an indicator of a chemical's carcinogenic potential.

Listings of all published NTP reports and ongoing studies are available from NTP Central Data Management, NIEHS, P.O. Box 12233, MD E1-02, Research Triangle Park, NC 27709 (919-541-3419). The Abstracts and other study information for 2-year studies are available at the NTP's World Wide Web site: http://ntp-server.niehs.nih.gov.

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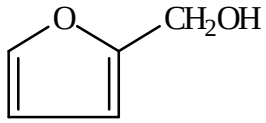
CONTENTS

ABSTRACT



FURFURYL ALCOHOL

CAS No. 98-00-0

Chemical Formula: $C_5H_6O_2$ Molecular Weight: 98.10

Synonyms: 2-Furancarbinol; 2-furanmethanol; furfuralcohol; α-furylcarbinol; 2-furylcarbinol; 2-hydroxymethylfuran

Furfuryl alcohol-based resins are used as binding agents in foundry sand and as corrosion inhibitors in mortar, grout, and cement. Because of their heat resistance, furan resins are used in the manufacture of fiberglass-reinforced plastic equipment. Furfuryl alcohol was selected for evaluation because of the absence of data on its carcinogenic potential and its large production volume, widespread use in manufacturing, and ubiquitous presence in consumer goods. Male and female F344/N rats and B6C3F$_1$ mice were exposed to furfuryl alcohol (greater than 98% pure) by inhalation for 16 days, 14 weeks, or 2 years. Genetic toxicology studies were conducted in *Salmonella typhimurium*, cultured Chinese hamster ovary cells, and mouse bone marrow cells.

16-DAY STUDY IN RATS

Groups of five male and five female rats were exposed to concentrations of 0, 16, 31, 63, 125, or 250 ppm furfuryl alcohol by inhalation, 6 hours per day, 5 days per week for 16 days. All male and female rats exposed to 250 ppm died by day 2 of the study, and one male rat exposed to 125 ppm died on day 5. Final mean body weights of male and female rats exposed to 125 ppm were significantly less than those of the chamber control groups. Male rats exposed to 31, 63, or 125 ppm and female rats exposed to 125 ppm gained less weight than the chamber control groups. Clinical findings included dyspnea, hypoactivity, and nasal and ocular discharge in males and females exposed to 63, 125, or 250 ppm. All exposed animals developed lesions in the nasal respiratory epithelium and olfactory epithelium, and the severities of these lesions generally increased with increasing exposure concentration.

16-DAY STUDY IN MICE

Groups of five male and five female mice were exposed to concentrations of 0, 16, 31, 63, 125, or 250 ppm furfuryl alcohol by inhalation, 6 hours per day, 5 days per week for 16 days. All male and female mice exposed to 250 ppm died by day 4 of the study, and one female mouse exposed to 125 ppm died on day 14. Mean body weights of male and female mice exposed to 63 or 125 ppm were significantly less than those of the chamber control groups. All exposed animals except one 16 ppm male developed lesions in the nasal respiratory epithelium and/or olfactory epithelium, and the severities of these lesions generally increased with increasing exposure concentration.

14-WEEK STUDY IN RATS

Groups of 10 male and 10 female rats were exposed to furfuryl alcohol at concentrations of 0, 2, 4, 8, 16, or 32 ppm, 6 hours per day, 5 days per week for 14 weeks. All rats survived to the end of the study. The mean body weight gain of females exposed to 32 ppm was less than that of the chamber control group. Exposure-related increases in the incidences of squamous metaplasia of the respiratory and transitional epithelium, goblet cell hyperplasia of the respiratory epithelium, and hypertrophy of the respiratory epithelium lining the nasopharyngeal duct were observed in the nose of male and female rats. The incidences of degeneration, hyperplasia, metaplasia, and surface exudate of the olfactory epithelium generally increased with increasing exposure concentration in males and females.

14-WEEK STUDY IN MICE

Groups of 10 male and 10 female mice were exposed to furfuryl alcohol at concentrations of 0, 2, 4, 8, 16, or 32 ppm, 6 hours per day, 5 days per week for 14 weeks. All mice survived to the end of the study. Heart weights of 32 ppm males were significantly less than those of the chamber controls. Exposure-related histologic changes included degeneration, metaplasia, and chronic inflammation of the olfactory epithelium; hyaline droplets of the respiratory epithelium; and squamous metaplasia of the submucosal gland of the cuboidal epithelium in males and females.

2-YEAR STUDY IN RATS

Groups of 50 male and 50 female rats were exposed to furfuryl alcohol by inhalation, 6 hours per day, 5 days per week for 105 weeks, at concentrations of 0, 2, 8, or 32 ppm.

Survival and Body Weights

All male rats exposed to 32 ppm died by week 99; survival of all other exposed groups of male and female rats was similar to that of the chamber control groups. Mean body weights of 32 ppm males were less than those of the chamber control group beginning at week 19.

Pathology Findings

All groups of exposed male and female rats had significantly increased incidences of nonneoplastic histologic changes of the nose compared to the chamber control groups. An adenoma of the lateral wall of the nose was observed in one 2 ppm male and one 8 ppm female, an adenoma of the respiratory epithelium was observed in one 8 ppm male and one 32 ppm female, one carcinoma of the respiratory epithelium was observed in a 32 ppm male, and squamous cell carcinomas of the nose were observed in three 32 ppm males. Renal tubule adenomas were present in one chamber control male, one 2 ppm male, two 8 ppm males, and two 32 ppm females. One 2 ppm female had a renal tubule carcinoma. Additional histologic sections from the kidney revealed the presence of additional hyperplasias in all groups of males and females; one additional renal tubule adenoma was observed in each of the chamber control, 2 ppm, and 8 ppm male groups, and four additional adenomas were observed in 32 ppm males. In females, two additional adenomas were found in the 8 ppm group, one adenoma in the 32 ppm group, and one carcinoma in the 2 ppm group. The severities of nephropathy relative to the chamber controls were increased in 32 ppm males and females. Males exposed to 32 ppm had extrarenal signs indicative of marked nephropathy including parathyroid gland hyperplasia and fibrous osteodystrophy.

2-YEAR STUDY IN MICE

Groups of 50 male and 50 female mice were exposed to furfuryl alcohol by inhalation, 6 hours per day, 5 days per week for 105 weeks, at concentrations of 0, 2, 8, or 32 ppm.

Survival, Body Weights, and Clinical Findings

Survival of exposed males and females was similar to that of the chamber control groups. Mean body weights of exposed males were generally similar to those of the chamber control group throughout the study. Mean body weights of exposed females were less than those of the chamber control group during year 2 of the study. Female mice exposed to 32 ppm developed focal corneal opacities.

Pathology Findings

The incidences of renal tubule neoplasms were increased in 32 ppm male mice compared to the chamber control group and exceeded the historical control range for inhalation studies. Step sectioning revealed the presence of additional hyperplasias in the chamber control and exposed groups and one adenoma in 32 ppm males. The severity of nephropathy increased with increasing exposure concentration in male mice. The incidence of renal tubule degeneration in male mice exposed to 32 ppm was significantly greater than in the chamber control group. Incidences of a variety of nonneoplastic lesions of the nose were significantly greater in all exposed groups of male and female mice than in the chamber control groups. The incidence of degeneration of the cornea was significantly greater in 32 ppm female mice compared to the chamber control group.

GENETIC TOXICOLOGY

Furfuryl alcohol was not mutagenic in *Salmonella typhimurium* strain TA98, TA100, TA1535, or TA1537, with or without S9. It did induce sister chromatid exchanges in cultured Chinese hamster ovary cells in the absence of S9, but not in the presence of S9. No induction of chromosomal aberrations was noted in cultured Chinese hamster ovary cells treated with furfuryl alcohol in the absence of S9, but in the presence of S9 an equivocal result was obtained. *In vivo*, no induction of sister chromatid exchanges, chromosomal aberrations, or micronuclei was noted in bone marrow cells of male mice after treatment with furfuryl alcohol.

CONCLUSIONS

Under the conditions of these 2-year inhalation studies, there was *some evidence of carcinogenic activity** of furfuryl alcohol in male F344/N rats based on increased incidences of combined neoplasms of the nose. There was *equivocal evidence of carcinogenic activity* of furfuryl alcohol in female F344/N rats based on marginally increased incidences of neoplasms of the nose and renal tubule neoplasms. There was *some evidence of carcinogenic activity* of furfuryl alcohol in male B6C3F_1 mice based on increased incidences of renal tubule neoplasms. There was *no evidence of carcinogenic activity* of furfuryl alcohol in female B6C3F_1 mice exposed to 2, 8, or 32 ppm.

Exposure of male and female rats and male mice to furfuryl alcohol was associated with increased incidences of nonneoplastic lesions of the nose and increased severities of nephropathy. Exposure of female mice to furfuryl alcohol was associated with increased incidences of nonneoplastic lesions of the nose and corneal degeneration.

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* Explanation of Levels of Evidence of Carcinogenic Activity is on page 10. A summary of the Technical Reports Review Subcommittee comments and the public discussion on this Technical Report appears on page 12.

Summary of the 2-Year Carcinogenesis and Genetic Toxicology Studies of Furfuryl Alcohol

	Male F344/N Rats	Female F344/N Rats	Male $B6C3F_1$ Mice	Female $B6C3F_1$ Mice
Concentrations in air	0, 2, 8, or 32 ppm	0, 2, 8, or 32 ppm	0, 2, 8, or 32 ppm	0, 2, 8, or 32 ppm
Body weights	32 ppm group less than chamber control group	Exposed groups similar to chamber control group	Exposed groups similar to chamber control group	Exposed groups less than chamber control group
Survival rates	8/50, 5/50, 9/50, 0/50	26/50, 26/50, 22/49, 16/50	34/50, 36/50, 30/50, 38/50	34/50, 33/49, 32/50, 40/50
Nonneoplastic effects	Nose (all sites): suppurative inflammation (3/50, 6/50, 17/50, 44/50); glands, hyperplasia (0/50, 0/50, 22/50, 49/50); lateral wall hyperplasia (1/50, 49/50, 50/50, 50/50); lateral wall, squamous metaplasia (1/50, 1/50, 8/50, 33/50) Nose (olfactory epithelium): atrophy (1/50, 12/50, 47/50, 50/50); hyaline degeneration (42/50, 48/50, 50/50, 47/50); fibrosis (0/50, 1/50, 26/50, 40/50); hyperplasia (0/50, 1/50, 42/50, 40/50); metaplasia (1/50, 8/50, 37/50, 49/50) Nose (respiratory epithelium): hyaline degeneration (12/50, 14/50, 45/50, 3/50); hyperplasia (0/50, 26/50, 50/50, 50/50); squamous metaplasia (0/50, 0/50, 3/50, 26/50) Kidney (all sites): severity of nephropathy (2.9, 2.9, 3.1, 3.7)	Nose (all sites): suppurative inflammation (4/49, 1/50, 5/48, 23/49); glands, hyperplasia (0/49, 0/50, 24/48, 46/49); lateral wall hyperplasia (0/49, 39/50, 48/48, 49/49); lateral wall, squamous metaplasia (0/49, 1/50, 0/48, 24/49) Nose (olfactory epithelium): atrophy (0/49, 6/50, 44/48, 49/49); hyaline degeneration (43/49, 50/50, 47/48, 48/49); fibrosis (0/49, 0/50, 16/48, 31/49); hyperplasia (0/49, 0/50, 31/48, 41/49); metaplasia (0/49, 5/50, 37/48, 48/49) Nose (respiratory epithelium): hyaline degeneration (23/49, 39/50, 45/48, 6/49); hyperplasia (0/49, 18/50, 40/48, 49/49); squamous metaplasia (0/49, 0/50, 2/48, 10/49) Kidney (all sites): severity of nephropathy (1.9, 1.9, 1.9, 2.4)	Nose (all sites): suppurative inflammation (7/50, 11/49, 27/49, 28/50); glands, hyperplasia (0/50, 10/49, 48/49, 46/50); glands, squamous metaplasia (0/50, 6/49, 35/49, 47/50); lateral wall, squamous metaplasia (0/50, 9/49, 10/49, 20/50) Nose (olfactory epithelium): atrophy (3/50, 15/49, 49/49, 50/50); hyaline degeneration (2/50, 3/49, 21/49, 39/50); metaplasia (0/50, 12/49, 49/49, 50/50) Nose (respiratory epithelium): hyaline degeneration (5/50, 18/49, 42/49, 45/50); squamous metaplasia (0/50, 2/49, 10/49, 20/50); regeneration (0/50, 1/49, 13/49, 21/50) Kidney (all sites): severity of nephropathy (1.2, 1.4, 1.5, 1.8)	Nose (all sites): suppurative inflammation (5/50, 12/48, 25/49, 42/50); glands, hyperplasia (0/50, 33/48, 46/49, 47/50); glands, squamous metaplasia (1/50, 1/48, 34/49, 46/50); lateral wall, squamous metaplasia (3/50, 14/48, 16/49, 36/50) Nose (olfactory epithelium): atrophy (2/50, 35/48, 49/49, 50/50); hyaline degeneration (7/50, 14/48, 28/49, 45/50); metaplasia (0/50, 31/48, 49/49, 49/50) Nose (respiratory epithelium): hyaline degeneration (19/50, 44/48, 49/49, 48/50); squamous metaplasia (1/50, 9/48, 21/49, 39/50); regeneration (0/50, 0/48, 9/49, 13/50) Eye: cornea, degeneration (3/49, 1/49, 4/49, 26/50)
Neoplastic effects	Nose (all sites): adenoma, carcinoma, or squamous cell carcinoma (0/50, 1/50, 1/50, 4/50)	None	Kidney (renal tubule): adenoma (standard evaluation - 0/50, 0/49, 0/49, 2/50; standard and extended evaluations combined - 0/50, 0/49, 0/49, 3/50); carcinoma (standard evaluation - 0/50, 0/49, 0/49, 2/50; standard and extended evaluations combined - 0/50, 0/49, 0/49, 2/50); adenoma or carcinoma (standard evaluation - 0/50, 0/49, 0/49, 4/50; standard and extended evaluations combined - 0/50, 0/49, 0/49, 5/50)	None

Summary of the 2-Year Carcinogenesis and Genetic Toxicology Studies of Furfuryl Alcohol

	Male F344/N Rats	Female F344/N Rats	Male $B6C3F_1$ Mice	Female $B6C3F_1$ Mice
Uncertain findings	None	Nose (all sites): lateral wall, adenoma (0/49, 0/50, 1/48, 0/49) Nose (respiratory epithelium): adenoma (0/49, 0/50, 0/48, 1/49); lateral wall, adenoma (0/49, 0/50, 1/48, 0/49) Kidney (renal tubule): adenoma (standard evaluation - 0/50, 0/49, 0/49, 2/50; standard and extended evaluations combined - 0/50, 0/49, 2/49, 2/50); carcinoma (standard evaluation - 0/50, 1/49, 0/49, 0/50; standard and extended evaluations combined - 0/50, 1/49, 0/49, 0/50); adenoma or carcinoma (standard evaluation - 0/50, 1/49, 0/49, 2/50; standard and extended evaluations combined - 0/50, 1/49, 2/49, 2/50)	None	None
Level of evidence of carcinogenic activity	Some evidence	Equivocal evidence	Some evidence	No evidence
Genetic toxicology				
Salmonella typhimurium gene mutations:		Negative in strains TA98, TA100, TA1535, and TA1537 with and without S9		
Sister chromatid exchanges				
Cultured Chinese hamster ovary cells *in vitro*:		Positive without S9; negative with S9		
Mouse bone marrow *in vivo*:		Negative		
Chromosomal aberrations				
Cultured Chinese hamster ovary cells *in vitro*:		Negative without S9; equivocal with S9		
Mouse bone marrow *in vivo*:		Negative		
Micronucleated erythrocytes				
Mouse bone marrow *in vivo*:		Negative		

EXPLANATION OF LEVELS OF EVIDENCE OF CARCINOGENIC ACTIVITY

The National Toxicology Program describes the results of individual experiments on a chemical agent and notes the strength of the evidence for conclusions regarding each study. Negative results, in which the study animals do not have a greater incidence of neoplasia than control animals, do not necessarily mean that a chemical is not a carcinogen, inasmuch as the experiments are conducted under a limited set of conditions. Positive results demonstrate that a chemical is carcinogenic for laboratory animals under the conditions of the study and indicate that exposure to the chemical has the potential for hazard to humans. Other organizations, such as the International Agency for Research on Cancer, assign a strength of evidence for conclusions based on an examination of all available evidence, including animal studies such as those conducted by the NTP, epidemiologic studies, and estimates of exposure. Thus, the actual determination of risk to humans from chemicals found to be carcinogenic in laboratory animals requires a wider analysis that extends beyond the purview of these studies.

Five categories of evidence of carcinogenic activity are used in the Technical Report series to summarize the strength of the evidence observed in each experiment: two categories for positive results (**clear evidence** and **some evidence**); one category for uncertain findings (**equivocal evidence**); one category for no observable effects (**no evidence**); and one category for experiments that cannot be evaluated because of major flaws (**inadequate study**). These categories of interpretative conclusions were first adopted in June 1983 and then revised in March 1986 for use in the Technical Report series to incorporate more specifically the concept of actual weight of evidence of carcinogenic activity. For each separate experiment (male rats, female rats, male mice, female mice), one of the following five categories is selected to describe the findings. These categories refer to the strength of the experimental evidence and not to potency or mechanism.

- **Clear evidence** of carcinogenic activity is demonstrated by studies that are interpreted as showing a dose-related (i) increase of malignant neoplasms, (ii) increase of a combination of malignant and benign neoplasms, or (iii) marked increase of benign neoplasms if there is an indication from this or other studies of the ability of such tumors to progress to malignancy.
- **Some evidence** of carcinogenic activity is demonstrated by studies that are interpreted as showing a chemical-related increased incidence of neoplasms (malignant, benign, or combined) in which the strength of the response is less than that required for clear evidence.
- **Equivocal evidence** of carcinogenic activity is demonstrated by studies that are interpreted as showing a marginal increase of neoplasms that may be chemical related.
- **No evidence** of carcinogenic activity is demonstrated by studies that are interpreted as showing no chemical-related increases in malignant or benign neoplasms.
- **Inadequate study** of carcinogenic activity is demonstrated by studies that, because of major qualitative or quantitative limitations, cannot be interpreted as valid for showing either the presence or absence of carcinogenic activity.

When a conclusion statement for a particular experiment is selected, consideration must be given to key factors that would extend the actual boundary of an individual category of evidence. Such consideration should allow for incorporation of scientific experience and current understanding of long-term carcinogenesis studies in laboratory animals, especially for those evaluations that may be on the borderline between two adjacent levels. These considerations should include:

- adequacy of the experimental design and conduct;
- occurrence of common versus uncommon neoplasia;
- progression (or lack thereof) from benign to malignant neoplasia as well as from preneoplastic to neoplastic lesions;
- some benign neoplasms have the capacity to regress but others (of the same morphologic type) progress. At present, it is impossible to identify the difference. Therefore, where progression is known to be a possibility, the most prudent course is to assume that benign neoplasms of those types have the potential to become malignant;
- combining benign and malignant tumor incidence known or thought to represent stages of progression in the same organ or tissue;
- latency in tumor induction;
- multiplicity in site-specific neoplasia;
- metastases;
- supporting information from proliferative lesions (hyperplasia) in the same site of neoplasia or in other experiments (same lesion in another sex or species);
- presence or absence of dose relationships;
- statistical significance of the observed tumor increase;
- concurrent control tumor incidence as well as the historical control rate and variability for a specific neoplasm;
- survival-adjusted analyses and false positive or false negative concerns;
- structure-activity correlations; and
- in some cases, genetic toxicology.

NATIONAL TOXICOLOGY PROGRAM BOARD OF SCIENTIFIC COUNSELORS
TECHNICAL REPORTS REVIEW SUBCOMMITTEE

The members of the Technical Reports Review Subcommittee who evaluated the draft NTP Technical Report on furfuryl alcohol on 10 December 1997 are listed below. Subcommittee members serve as independent scientists, not as representatives of any institution, company, or governmental agency. In this capacity, subcommittee members have five major responsibilities in reviewing the NTP studies:

- to ascertain that all relevant literature data have been adequately cited and interpreted,
- to determine if the design and conditions of the NTP studies were appropriate,
- to ensure that the Technical Report presents the experimental results and conclusions fully and clearly,
- to judge the significance of the experimental results by scientific criteria, and
- to assess the evaluation of the evidence of carcinogenic activity and other observed toxic responses.

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SUMMARY OF TECHNICAL REPORTS REVIEW SUBCOMMITTEE COMMENTS

On 10 December 1997 the draft Technical Report on the toxicity and carcinogenicity studies of furfuryl alcohol received public review by the National Toxicology Programs's Board of Scientific Counselor's Technical Reports Review Subcommittee. The review meeting was held at the National Institute of Environmental Health Sciences, Research Triangle Park, NC.

Dr. R.D. Irwin, NIEHS, introduced the toxicity and carcinogenesis studies of furfuryl alcohol by discussing the uses of the chemical and the rationale for study, describing the experimental design, reporting on survival and body weight effects, and commenting on compound-related neoplastic and nonneoplastic lesions in rats and mice. The proposed conclusions for the 2-year studies were *some evidence of carcinogenic activity* in male F344/N rats and male B6C3F$_1$ mice, *equivocal evidence of carcinogenic activity* in female F344/N rats, and *no evidence of carcinogenic activity* in female B6C3F$_1$ mice.

Drs. Cullen and J. Russo, principal reviewers, agreed with the proposed conclusions.

Dr. Bus, a principal reviewer, agreed with the proposed conclusions. He noted that the proposed conclusion for female rats was partly based on the observation of renal tubule neoplasms, particularly when they are observed in extended evaluation step sections. Dr. Bus also noted that the proposed conclusion for male mice was based entirely on the same observation. He stated that it is unclear whether the neoplasms observed in the step sections were new or the same neoplasms observed in the standard evaluation (see p. 43). Dr. Bus commented that more attention should have been paid to the 14-week rat study results in setting exposure concentrations for the 2-year study, in that 32 ppm appeared to exceed the maximum tolerated dose and 2 ppm was above the no-effect level. Dr. Irwin said that in setting exposure concentrations for the 2-year study, mean body weights at 32 ppm were within 10% of the controls and the shape of the growth curve indicating this would probably not change much or that these animals might recover. In the 2-year study, mean body weights of 32 ppm female rats were observed to be approximately the same as those of the chamber controls.

Dr. Carlson commented on the rationale for studying furfuryl alcohol as part of a class study with furan and furfural, noting that cholangiocarcinomas and other hepatocellular neoplasms were significant neoplastic findings with furan and furfural. He noted that no liver response was seen with furfuryl alcohol in contrast with the other two analogues. Dr. Bailer said he thought the proposed level of evidence in male rats should have been *clear evidence of carcinogenic activity* based on an exposure-related response and four malignant neoplasms in the high exposure group. Dr. J.K. Haseman, NIEHS, said that although there were no squamous cell carcinomas of the nose in the chamber control groups for inhalation studies, there have been one or two in some control groups in other concurrent studies. Dr. Irwin said that the lack of supporting data in females also entered into the decision to go with the proposed conclusion of *some evidence of carcinogenic activity* for male rats.

Dr. Bus moved that the Technical Report on furfuryl alcohol be accepted with the revisions discussed and the conclusions as written for male rats and mice, *some evidence of carcinogenic activity*; for female rats, *equivocal evidence of carcinogenic activity*; and for female mice, *no evidence of carcinogenic activity*. Dr. Cullen seconded the motion, which was accepted by six yes votes to two no votes (Drs. Bailer and Goldsworthy).